REMARKS

The Official Action of February 19, 2009 and the references cited therein have been carefully considered. The remarks herein are considered responsive thereto. Claims 17-19, 21, 22, 27 and 28 remain in the case.

Claims 17-19, 21, 24, and 26 are rejected under 35 USC 103(a) as being unpatentable over WO01/46140 in view of WO02/24647. The Examiner states that WO01/46140 discloses E2 prostaglandins for preventing bone loss but lacks the 4,4 difluoro substitution and WO02/24647 discloses agonists of the EP4 subtype useful in the prevention of bone loss, where the difference constitutes a carboxylic acid terminus to the alpha chain in place of the instantly claimed 1H-tetrazol-5-yl group. While Examiner concedes that he could not find overlap between the Examples of the reference and Applicant's claimed compounds, he contends that the "claimed compounds and that disclosed in WO01/46140 and WO02/24647 represent straightforward cases of bioisoterism" and that one of ordinary skill in the art would be motivated to modify the compounds of WO01/46140 and WO02/24647 with other substituents to arrive at the instant compounds for use in treating bone disorders."

A prima facie case of obviousness requires structural similarity between claimed and prior art subject matter and a showing of "adequate support in the prior art" for the change in structure to arrive at the claimed compounds. Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd., 492 F.3d 1350, 1356 (Fed. Cir. 2007) (internal citations omitted). This test is consistent with KSR, which requires identification of "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does" in an obviousness determination. Id. at 1356-1357, citing KSR International Co. v. Teleflex Inc., 127 S.Ct. 1727, 1731 (2007).

Applicants respectfully note that the compounds disclosed by WO01/46140 and WO02/24647 are not structurally similar to compounds of the instant invention. As the Examiner indicates, WO01/46140 is directed at EP4 receptor agonists which lacks the 4,4 difluoro substituent required by the claimed invention. Likewise, WO02/24647 is directed to EP4 receptor agonists that lack the tetrazole substituent on the alpha terminus. The compounds of the present invention is directed toward compounds in which the alpha terminus is always a tetrazole and a 4,4 difluoro substituent is always present. Thus, the claimed invention is patentable over WO01/46140 and WO02/24647 because the compounds disclosed in the references are not structurally similar to the claimed compounds.

Chemical obviousness requires that one skilled in the art would have had a reason to make specific structural changes to arrive at the compounds of the present invention, useful for the treatment of intraocular pressure. See Takeda, 492 F.3d at 1356. Even if the compounds of the present invention were structurally similar to those disclosed in WO01/46140 and WO02/24647, the Examiner has not indicated any reason one would have been motivated by the disclosure in WO01/46140 and WO02/24647 to make the specific structural changes necessary to arrive at the compounds of the instant invention for use in treating intraocular pressure.

Also, obviousness requires that the skilled artisan would have had a reasonable expectation of success in making a suggested modification. Pfizer v. Apotex, 450 F.3d 1348, 1361 (Fed. Cir. 2007). Here, the Examiner has not stated why one skilled in the art would have reasonably expected that modifying the compounds of WO01/46140 and WO02/24647 to arrive at the compounds of the present invention would produce compounds that are able to significantly improve EP4 affinity, and are highly selective against other prostanoid receptors. As shown on page 50, lines 22-32, of the specification, Example 7 is a "high affinity ligand at the EP4 receptor with a binding affinity in the range of 0.2-2 nM ...and was also highly selective against other prostanoid receptors with binding affinities greater than 2 μM".

Even if the Examiner contends that suggestion or motivation is implicit in the prior art, the Examiner must support his contention with "particular findings" rather than "conclusory statements." See, e.g., In re Kotzab, 217 F.3d 1365, 1370 (Fed. Cir. 2000). An examiner's assessment of "basic knowledge" or "common sense" still requires supporting evidence in order to be the basis of an obviousness rejection. In re Zurko, 258 F.3d 1379, 1385 (Fed. Cir. 2001).

Thus, Applicants respectfully contend that the claims at hand are nonobvious over WO01/46140 and WO02/24647 and request reconsideration of Claims 17-19.

Claims 21, 22, 27, and 28 are also rejected under 35 USC 103(a) as being unpatentable over WO01/46140 and WO02/24647 as applied to claims 17 as indicated above, and further in view of WO00/38667. The Examiner suggests that because WO00/38667 describes the use of EP receptor agonists in combination with beta-blockers in the reduction of intraocular pressure that when combined with WO01/46140 and WO02/24647 one of ordinary skill in the art would be motivated to employ the compounds of WO01/46140 as modified by WO02/24647 in combination with a beta blocker to arrive at a composition capable of treating glaucoma .

Applicants respectfully reply that the compounds of the present invention are not obvious over WO01/46140 or WO02/24647, either alone or in combination, because they

are structurally distinct. As stated above, neither WO01/46140 or WO02/24647 teach or suggest compounds having a tetrazole on the alpha terminus and a 4,4 difluoro substituent, that provide compounds that have a significantly high affinity for the EP4 receptor and are highly selective against other prostanoid receptors. Thus, one of ordinary skill in the art would not have been motivated to combine the teaching of WO00/38667 with WO01/46140 and WO02/24647 to arrive at the specifically claimed compounds with the unique properties for use in treating glaucoma.

Even if the compounds of WO01/46140 and WO02/24647 and the present invention were structurally similar, the Examiner has not cited any support for his assertion that one skilled in the art would have been motivated by the disclosures of WO01/46140, WO02/24647 to make the specific modifications necessary to arrive at the specifically claimed compounds with the unique properties for use in treating glaucoma.. Nor has he cited any reason why one would have had a reasonable expectation, based on the disclosure of WO01/46140 and WO02/24647 that the instant compounds would be effective in the treatment of glaucoma.

In light of the remarks herein Applicants believe the claims are in condition for allowance. The Examiner is respectfully requested to contact the undersigned at the number below if this would expedite the allowance.

Respectfully submitted,

By: _____

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